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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,797	11/23/2001	George Jackowski	2132.084	5616

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 11/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,797	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *3-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/12/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-2 are drawn to a biopolymer having SEQ ID NO: 1 or SEQ ID NO:2, classified in class 530, subclass 300 or class 530, subclass 350 for example.

II. Claims 3-9, 18-28 and 33-38 are drawn to methods and kits which not only detect SEQ ID NO: 1 or SEQ ID NO:2, further requiring a correlation to disease state, diagnosing, therapeutic avenues, an/or risk assessment, classified in class 436, subclass 518 and class 424, subclass 93.1 for example.

III. Claims 10-17 are drawn to kit for merely detecting SEQ ID NO: 1 or SEQ ID NO:2, classified in class 422, subclass 61 for example.

IV. Claims 29-32 are drawn to antibodies that bind SEQ ID NO: 1 or SEQ ID NO:2, classified in class 530, subclass 387.1/387.2 and class 424, subclass 130.1 for example.

2. The inventions are distinct, each from the other because of the following reasons:

A. Inventions **I and IV** are drawn to two disclosed patentably distinct inventions (compositions comprising materially different limitations).

Group I is directed to a biopolymer while Group IV is directed to antibodies with specificity for the biopolymer. The two products are independent and require different searches. These separate products/compositions bear distinct structural or biochemical properties **Therefore, each disclosed patentably distinct composition is considered a separate invention.**

B. The method/kit inventions of Group **II** and **III** are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventive methods/kits are patentably distinct. Group II *merely detects* Seq Id No: 1 or Seq Id No: 2, while Group III is drawn to methods/kits that *include* Seq Id No: 1 or 2 and further correlates the detection to disease state assessment, product regulation, and therapeutic evaluations. The addition of the biopolymers or the additional correlation is not required in the kit of invention II. Therefore the methods/kits utilize different reagents and have different method steps (different modes of operation/function/effects).

C. Inventions **(I and IV)** and **(II and III)** are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case each of the products (I and IV) are materially different and can be used in any of the materially different processes/kits of invention II and III.

It is recognized that although the search for the inventions may overlap they are not totally co-extensive, where the search for one would fully encompass the search for the others. Because these inventions are distinct for the reasons given above and the search required for Inventions I-IV are not mutually inclusive (i.e. the search for one invention is not required for the other inventions) restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

3. The inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Please note that the classifications in the restriction are illustrative only and **do not** represent all the classes and subclasses which must be searched for each invention; nor is the search limited to issued US patents, but rather includes foreign patents and applications as well as literature searches.

4. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement is traversed (37 CFR 1.143).

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventor ship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventor ship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

6. During a telephone conversation with Ferris H. Lander (43,377) on 8/6/04 a provisional election was made with traverse to prosecute the invention of Group I, claim 1. Affirmation of this election must be made by applicant in replying to this Office action. Claims 3-38 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

7. The instant application does not claim priority or benefits to an earlier application.

Information Disclosure Statement

8. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the Examiner on form PTO-892 or Applicant on form PTO-1449 has cited the references they have not been considered.

9. The information disclosure statements filed March 12, 2002 has been considered as to the merits prior to first action.

Oath/Declaration

10. A new oath or declaration is required because the oath submitted 11/23/01 is not signed by the inventors. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Specification

11. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

I. On page 1 line 23 a typo appears. A "))" is missing. Please add.

II. The use of the trademarks has been noted in this application. (i.e. SEPHAROSE on page 41 lines 2 and 3, TRITON on page 42 line 10). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Abstract

12. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited.

The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

13. The instant application includes legal phraseology "said". Appropriate correction is required.

Sequence Non-Compliance

14. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132. The disclosure contains sequences that have not been appropriately identified by sequence identification numbers, see page 46.

Applicant is given THREE MONTHS from the mailing date of this communication within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g).

Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to comply with the reply.

Claim Objections

15. Claims 1 and 2 are objected to under 37CFR 1.821(d) for failing to recite SEQ ID NOS in the claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1 and 2 are vague and indefinite because it is unclear as to what the term "at least one analyte thereof" is intended to define. The claim is directed to biopolymers consisting of SEQ ID NO 1 and SEQ ID NO 2. However what is considered an analyte of SEQ ID NO 1 or 2 is not defined by the claims or the specification. As recited the metes and bounds of the claims cannot be determined and one of ordinary skill in the art would not be appraised of the scope of the instant invention. Please explain/correct.

B. Claims 1 and 2 are vague and indefinite because the biopolymer is "indicative" of at least one particular disease state in claim 1 and "predictive of" Alzheimer's disease in claim 2. "Indication" and "predictability" are relative term, which render the claims indefinite. The terms are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear as to how the measurement of the biopolymer marker will further serve to indicate a particular disease state or predict Alzheimer's disease. It is suggested that the claim merely recite "detection of" Alzheimer's disease.

Further it is not clear as to how the marker will identify Alzheimer's disease because a correlation of the markers with Alzheimer's in not disclosed in the specification. Please clarify.

C. Claim 1 is vague and indefinite because it is not clear as to what the symbol (-) is intended to mean. The symbol is included in the amino acid sequence consisting of XSVLTQPPSVSGAPGQR(V). Is this a typo or does applicant intend to include other amino acids, which have not been clearly defined? Appropriate correction is required but must not introduce new matter into the specification.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

17. Claims 1 and 2 are directed to non-statutory subject matter. The invention as claimed read on any biopolymer makers consisting of SEQ ID NO:1, SEQ ID NO:2, or an analyte thereof wherein the analyte thereof would read on products of nature absent the isolation of said analyte thereof. Non-naturally occurring compositions are considered to be patentable subject matter within the scope of 35 U.S.C. 101. Compositions that are products of nature are considered non-statutory and non-patentable. See Official Gazette, 1077 O.G. 24, April 21, 1987. It is recommended that the claims incorporate the claim language, "isolated" or "purified" to overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

Claims 1 and 2 are directed to biopolymers consisting of SEQ ID NO:1 and SEQ ID NO:2 indicative of Alzheimers disease. However, the specification does not support this assertion. The specification (in particular page 46) and figures do not definitively correlate the claimed markers consisting of SEQ ID NO:1 or SEQ ID NO:2 to Alzheimer's disease.

Specifically, the specification recites that biopolymers consisting of SEQ ID NO:1 and SEQ ID NO:2 were found in the serum of patients suffering from Alzheimers disease on page 46 but does not contain any data supporting this contention and the figures do not identify SEQ ID NO:1 or SEQ ID NO:2 (Y14737 or X91133). Therefore it is unclear how SEQ ID NO:1 and SEQ ID NO:2 were identified as "notable sequences" or how they were deemed "evidentiary" of a disease state. There is nothing in the disclosure that would enable one to choose SEQ ID NO:1 or SEQ ID NO:2 as notable sequences among an infinite number of possible proteins or peptides present in a patient sample. There is no correlation between the procedure for screening samples from patients suspected of having a variety of different disease, the presence/absence of SEQ ID NO:1 or SEQ ID NO:2, and the determination, prediction, assessment of at least one particular disease state like Alzheimers disease.

Furthermore, Applicants have not provided any disclosure enabling the use of the biopolymer marker with regard to regulating the presence or absence of said sequence. The disclosure is equally lacking any teaching for how the identified sequence will be utilized to identify therapeutic avenues and regulate a disease state. There is no disclosure designating how the sequence could be utilized therein, enabling one of ordinary skill in the art to use the sequences in the diagnostic method.

Applicants have not set forth any supporting evidence that suggests that any of the sequences (SEQ ID NO: 1 or SEQ ID NO:2) are unique molecular markers for Alzheimer's disease or any other disease and the prior art teaches that disease markers are highly unpredictable and require extensive experimentation.

Hampel et al. (Journal of Neural Transmission, 2004, 11:247-272) disclose the difficulty involved in the discovery of marker candidates for Alzheimers. In this review, several critical criteria must be meet when determining a marker for Alzheimers. These include indication of disease progression, heterogeneity of the clinical population, as well as feasibility of testing. Also of concern are assay sensitivity, frequency of assessments, stability, standardization, dynamic range, and comparative analysis. See page 247-248 Summary.

Further, Tockman et al. (Cancer Research 52:2711s-2718s, 1992) teach considerations necessary for a suspected cancer biomarker (intermediate end point marker) to have efficacy and success in a clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other disorders.

Tockman teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials, see abstract. Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and **if validated** (emphasis added) can be used for population screening (p. 2713s, column 1).

The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease.

"This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point [marker]", see page 2714s, column 1, Biomarker Validation against Acknowledged Disease End Points section. Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials, see page 2716s, column 2, Summary section. Tockman reiterates that the predictability of the art in regards to cancer prognosis and the estimation of life expectancies within a population with a disease or disorder are highly speculative and unpredictable.

The instant disclosure has not addressed the issues taught in the prior art as crucial to the discovery of a biopolymer marker.

The nature of the invention- the invention is directed to disease markers or biopolymers.

The state of the prior art- the prior art of record fails to disclose the particular biopolymers in any disease state.

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the biopolymers are indicative of any disease state including Alzheimers disease.

The amount of direction or guidance present- appropriate guidance is not provided by the specification for the claimed biopolymers.

The presence or absence of working examples- working examples are not provided in the specification that exemplify the biopolymers as markers for any disease.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the biopolymers as claimed.

The relative skill of those in the art-the level of skill in the art is high.

The breadth of the claims- as recited, the instant claims are directed to biopolymers consisting of SEQ ID NO:1 or SEQ ID NO:2 being indicative of at least one disease state.

While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan that the breadth of the claimed biopolymer is enabled. This is not the case in the instant specification.

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue.

Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966). While every aspect of a generic claim does not have to be carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. Genetech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001. That requirement has not been met in this specification with respect to biopolymers consisting of SEQ ID NO:1 or SEQ ID NO:2 indicative of Alzheimers disease.

Therefore, in view of the insufficient guidance in the specification, extensive experimentation would be required to enable the claims and to practice the invention as claimed.

Double Patenting

19. Double patenting obviousness-type rejection:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 1 and 2 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1 and 2 of copending Application No. 09/993,304. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. SEQ ID NO:1 of application number 09/993,304 is the same as SEQ ID NO:2 in the instant application.

21. For reasons aforementioned, no claims are allowed.

22. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (703) 872-9306, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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